

The only rejections in this case are based on the assertion that the claimed combination of compounds would have been obvious over Phillippe.¹ However, even assuming Phillippe renders the claimed combination of compounds *prima facie* obvious – which it does not – Applicants’ showing of synergism is more than sufficient to rebut any such hypothetical case of *prima facie* obviousness.

In addition to the evidence already provided, Applicants have conducted further testing to demonstrate the synergistic properties of the claimed combination of compounds. Specifically, the depigmentation activity of combinations of compounds was determined using the techniques set forth in Example 1 of the present application. In accordance with the claimed invention, the depigmentation activity of N-cholesteryloxy carbonyl-4-para-aminophenol and hydroquinone, alone and in combination, was determined. These results are set forth below.

	% inhibition observed	% inhibition theoretical
Hydroquinone (8×10^{-5} M)	25	
N-cholesteryloxy carbonyl-4-para-aminophenol (6.77×10^{-5} M)	No detection	
Hydroquinone (8×10^{-5} M) + N-cholesteryloxy carbonyl-4-para-aminophenol (6.77×10^{-5} M)	31.8	24.4

¹ The Office Action rejected the pending claims under 35 U.S.C. § 103 as obvious over Phillippe’s PCT published application and under the doctrine of obviousness-type double patenting over Phillippe’s corresponding U.S. patent.

For purposes of comparison, the depigmentation activity of N-ethyloxycarbonyl-4-para-aminophenol and hydroquinone, alone and in combination, was determined. These results are set forth below.

	% inhibition observed	% inhibition theoretical
Hydroquinone (8×10^{-5} M)	26.12	
N-ethyloxycarbonyl-4-paraaminophenol (6.77×10^{-5} M)	13.64	
Hydroquinone (8×10^{-5} M) + N-ethyloxycarbonyl-4-para-aminophenol (6.77×10^{-5} M)	16.48	39.76

Thus, both experiments were performed using the same concentration of hydroquinone compound and of aminophenol compound in order to provide indisputably comparable results.

The claimed combination of hydroquinone and N-cholesteryloxycarbonyl-4-para-aminophenol resulted in synergistic inhibition activity (31.8% actual inhibition vs. 24.4% theoretical). In contrast, the combination of hydroquinone and N-ethyloxycarbonyl-4-paraaminophenol did not result in synergistic inhibition activity and, in fact, resulted in less than additive activity (16.48% actual inhibition vs. 39.76% theoretical).

The Office Action asserted that the examples in the present specification do not allow a comparison of the claimed combination of compounds with other combinations of compounds because of differing conditions in the examples (that is, different concentrations of compounds). While Applicants respectfully disagree with this assertion, Applicants have addressed the Office Action's concerns by performing the testing set forth above in which the testing conditions are the same. As confirmed by this new testing, the claimed combinations of compounds have synergistic anti-depigmentation activity.

In view of the above, Applicants respectfully submit that the examples in the present application as well as the testing discussed above are more than sufficient to demonstrate the novel, non-obvious, synergistic nature of the claimed combinations of compounds. Accordingly, Applicants respectfully submit that the pending rejections based upon Phillippe be withdrawn.

Applicants believe that the present application is in condition for allowance. Prompt and favorable consideration is earnestly solicited.

Respectfully submitted,

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A handwritten signature in black ink, appearing to read 'R. Treanor', with a long horizontal stroke extending to the right.

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